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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,113	12/22/2005	Guy Weinberg	27611/39002A	4295

4743 7590 07/15/2008

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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
07/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,113	WEINBERG ET AL.	
	Examiner	Art Unit	
	ALLISON M. FORD	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *10-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-9, in the reply filed on 4/16/2008 is acknowledged. Applicants made the election without prejudice, which is being understood as an election without traverse. (It is further noted Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, thus the election has been treated as an election without traverse (MPEP § 818.03(a)).) With regards to the election of species requirement, Applicants have elected "bupivacaine" from claim 5.

Claim 1-31 remain pending in the current application, of which claims 10-31 have been withdrawn as being directed to non-elected inventions. Claims 1-9 have been considered on the merits, claim 5 has been considered as far as it reads on the elected species bupivacaine.

Priority

The instant application is recognized as a national stage entry of PCT/US03/41605, having an international filing date of 12/31/2003, which further claims priority under 35 USC 119(e) to US Provisional application 60/437,200, filed 12/31/2002.

Specification/Abstract

The abstract submitted 6/29/2005 is objected to because the abstract does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). The amendment submitted on the same date is noted, yet this amended abstract still is presented on the same sheet as an amendment to the specification, and thus fails to comply with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Oath/Declaration

It is noted that Applicants have filed both an Application Data Sheet under 37 CFR 1.76 (on 6/29/2005) and a declaration under 37 CFR 1.63 (on 12/22/2005). Inconsistencies are noted with respect to the mailing address of the inventors between the information provided in the ADS and declaration. 37 CFR 1.76(d)(1) states that the latest submitted information will govern, notwithstanding whether supplied by and ADS or an amendment to the specification, a designation of a correspondence address, or by a § 1.63 or § 1.67 oath or declaration, except that the oath or declaration will govern inconsistencies with the ADS in the naming of inventors and setting forth their citizenship.

However, the declaration of 12/22/2005 is still considered defective because, while it sets forth the mailing address of each inventor, it does not clearly state that the inventor reside at the addresses at which they customarily receive mail. See 37 CFR 1.63(c)(1).

A supplemental oath or declaration in compliance with 37 CFR 1.67(a) or a supplemental Application Data sheet in compliance with 37 CFR 1.76 is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' claims are directed to a composition for protecting tissues or an organ of a mammal from damage when isolated from the circulatory system, comprising (a) a perfusion solution, and (b) an amount of an amphipathic compound that inhibits metabolism effective to protect the tissue or organ from damage to tissue anoxia, ischemia or reperfusion injury.

With regards to amphipathic compounds that inhibit metabolism effective to protect the tissue or organ from damage to tissue anoxia, ischemia, or reperfusion injury, it is submitted that Applicants have not provided sufficient written description to support the full genus of compounds claimed.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, **by functional characteristics coupled with a known or disclosed correlation between function and structure**, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

In the instant case the genus of compounds must have the shared function of being effective to inhibit metabolism to protect the tissue or organ from damage due to anoxia, ischemia or reperfusion injury, however, this common function has not been properly correlated with a specific physical and/or chemical structure. The only structural feature claims is that the compounds be 'amphipathic'; one of ordinary skill will clearly realize that all amphipathic compounds do not share the ability to inhibit metabolism in tissues an organs. Furthermore, with regards to the species currently disclosed (exemplified in claim 5), these species fail to represent the full scope of amphipathic compounds, but rather are limited to a small genus of local anesthetics. Thus, one of ordinary skill in the art, in looking to the instant specification, would not be able to determine that Applicants were in possession of the invention, as claimed, at the time the invention was made.

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Dobson (WO 00/56145).

Dobson discloses compositions suitable for use in arresting, protecting and/or preserving an organ. The composition generally includes (i) a potassium channel opener or antagonist and/or an adenosine receptor agonist and (ii) a local anesthetic (See Pg. 4, ln 10-13). The composition may further include a pharmaceutically acceptable carrier, dileunt, adjuvant and/or excipient (See Pg. 10, ln 1-3).

A preferred composition is disclosed in Example 1, comprising 100 uM adenosine and 0.5 mM lignocaine in Krebs-Henseleit buffer (See Pg. 16-17 "Example 1"). The solution is used as a cardioplegic solution, and is perfused into rat hearts to protects the organs during an arrest period.

The composition disclosed in Example 1 reads on the instantly claimed composition, as the Krebs-Henseleit buffer reads on the preservation solution, which is also the perfusion solution, and the lignocaine reads on an amphipathic compound that inhibits metabolism. It is submitted that the lignocaine is provided in an amount effective to protect the heart from significant damage due to tissue anoxia, ischemia and reperfusion injury, and to prevent lactic acidosis, as Dobson discloses hearts arrested with the disclosed solution were able to recover to near normal control values for heart rate, aortic pressure, aortic flow, coronary flow, cardiac output and O_2 consumption (See Table 1, Pg 18).

It is further noted that the instant specification references between 1 uM and 5 mM as suitable concentrations of the metabolic inhibitor for use in the instant composition (See Specification, Pg. 7); therefore, 0.5 mM, as disclosed by Dobson is considered to read on the instant invention.

It is noted that Dobson further states the disclosed composition can be used to protect a variety of other organs, including the brain, lung, kidney, and liver (See paragraph spanning pages 4-5).

Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dobson (WO 00/056145) as applied to claims 1-4, 8 and 9 above, and further in view of Pemberton-Goodman et al (WO 03/063782), the subject matter being relied upon is fully supported by US provisional

application 60/352,219 to Pemberton-Goodman et al (citations are directed to the WIPO document).

The teachings of Dobson are set forth above. Generally Dobson disclose an organ protectant and preservation composition comprising (i) a potassium channel opener or antagonist and/or an adenosine receptor agonist and (ii) a local anesthetic (See Dobson Pg. 4, ln 10-13), and further comprising a preservation solution as a pharmaceutically acceptable carrier (See Dobson, Pg 10, ln 1-3). The preferred embodiment of Dobson includes adenosine as the potassium channel opener, and lignocaine as the local anesthetic (See Dobson, Pg 16-17 "Example 1"). Dobson further discloses a number of local anesthetics which may be alternatively used in the composition, including lignocaine, mexiletine, diphenylhydantoin, prilocaine, procaine, mepavacaine and other Class 1B anti-arrhythmia drugs (See Dobson, paragraph spanning pages 6-7); however Dobson does not specifically disclose bupivacaine as a local anesthetic.

While Dobson does not specifically disclose bupivacaine, it is submitted that lignocaine and bupivacaine were taught in the art as functional equivalents with regards to their ability to function as local anesthetics useful in arresting, protecting and/or preserving hearts. In support see Pemberton-Goodman et al. Pemberton-Goodman et al disclose a composition suitable for arresting, protecting and/or preserving hearts, the composition of Pemberton-Goodman et al comprises k-PVIIA-related conotoxins as their active ingredient, and can further include local anesthetics, including lignocaine and bupivacaine (See Pemberton-Goodman et al, Pg 13, ln 1-19). Therefore, lignocaine and bupivacaine were both recognized in the art as local anesthetics each suitable for use in compositions for arresting, protecting, and/or preserving organs, including the heart, and thus substitution of bupivacaine for lignocaine in the composition of Dobson, to yield the predictable result of being suitable for organ preservation, would have been obvious to one of ordinary skill in the art at the time the invention was made.

With regards to the concentration of bupivacaine that may be employed in the composition of Dobson, it is noted that Dobson report using 0.5 mM of lignocaine (See Dobson, Pg 16-17, Example 1);

however Dobson states that the particular amounts and concentrations of each component of the solution will depend on the nature of the subject, the type of organ being arrested, and the proposed application. (See Dobson, Pg 8, ln 1-11). Therefore, while Dobson suggests use of anesthetics at the level claimed, it is submitted that the amount of bupivacaine or other anesthetic provided in the solution would be routinely optimized by one of ordinary skill in the art, in based on the nature of the subject, type of organ being arrested/protected/preserved, and the proposed application. Furthermore, in the absence of evidence showing that the claimed concentrations produce critical or unexpected results, the claimed conditions are considered to be merely optimized values, such values determinable by routine experimentation which was within the skill of the ordinary artisan. Please note generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical or produces unexpected results. "[W]here the general conditions of a claim are disclosed by the prior art it is not inventive to discover the optimum or workable ranges by routine experimentation" See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Examiner, Art Unit 1651